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ORIGINAL ARTICLES

Effect of artificial food colours on childhood behaviour

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Abstract

We performed an objective evaluation of 39 children whose behaviour was observed by their parents to improve on an artificial food additive free diet and to deteriorate with dietary lapses. Only 19 children completed a double blind placebo controlled challenge study with artificial food colours. In these children food colours were shown to have an adverse effect on a daily Conners' rating of behaviour, but most parents could not detect these changes. A pharmacological mechanism of food additive intolerance is proposed to explain these effects.

Ingestion of a number of artificial food additives has been shown to provoke urticaria[1] and asthma[2] in some individuals. The role of food additives in affecting children's behaviour is more controversial. Recent studies have been contradictory: one claimed that foods and food additives could provoke hyperactive behaviour in a group of very disturbed children with an unusually high incidence of atopy,[3] while another failed to show any such association.[4] These conflicting results are partly explained by methodological variations in trial design such as the use of placebos, the number of double blind challenges, and challenge doses.[5] Most trials only employed a single cross over design[3 4 6–10] when it has been argued that repeated cross over challenges are necessary to diagnose food intolerance.[11] One trial acknowledged a significant order effect that was difficult to explain.[3] We have been involved in a study of the prevalence and mechanism of 'organic' food additive intolerance,[12] and took the opportunity to investigate children whose parents believed that their behaviour was adversely affected by artificial food additives.

Patients and methods

SUBJECTS

Thirty nine children between the ages of 2·8 and 15·3 years (mean 8·9) were recruited from a paediatric allergy clinic and from a population survey of food additive intolerance.[12] Inclusion in the trial was based on the parents' observations that various behavioural problems had improved on a diet that eliminated food additives. The diet of these children excluded food additives to a variable extent, although all excluded artificial food colours. According to the parents, deliberate or inadvertent consumption of food additives, even in small amounts, precipitated the recurrence of their child's behavioural problems. The age of onset of these perceived food additive problems varied from less than 1 year to 9 years (mean 2·1) (table 1).

Parents stated that their children exhibited a variety of behavioural problems, which developed within several minutes, but occasionally up to 12 hours after consuming food additives. Poor concentration and excess fidgeting were identified as associated problems by most parents.

Most children attended normal schools, had no known neurological disorders, and had not received any psychiatric assessment. One child with idiopathic global retardation attended a school for the educationally subnormal, and one other child who had been diagnosed as being hyperkinetic and who had previously received methylphenidate was subsequently placed in a special school.

Children were included in the trial only if they were able to consistently swallow the size '0' capsules that contained the challenge material.

The parents were interviewed by IP using a standard questionnaire. The children underwent a general examination during which evidence of allergic disease was carefully sought. Skin prick tests to common allergens (cat, house dust mite, grass pollen, egg, milk) were performed to determine atopic state, and were considered positive if weals were greater than 3 mm after 10 minutes in the presence of positive histamine and negative saline controls.

STUDY PROTOCOL

For the duration of the trial, the food additive elimination diet of each child was maintained.

The trial consisted of double blind placebo controlled challenges with artificial food colours. The food colours chosen (tartrazine (E102) 50 mg, sunset yellow (E110) 25 mg, carmoisine (E122) 25 mg, and amaranth (E123)

Table 1 Clinical features (n=39)

Mean (range) age (years)	8·9 (2·8–15·3)
Sex (m:f)	29:10
No recruited from:	
Clinic	26
Population survey	13
No (%) with atopy	16 (41)
No (%) with atopic disease*	15 (38)
No (%) with other additive problems†	10 (26)
Mean (range) age of onset of additive intolerance (years)	2·1 (0–9)
Mean (range) reaction time after ingestion (hours)	2·5 (0–12)

*Asthma, eczema, or hay fever.
†Urticaria, gut upset, or headache.

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25 mg) are those most often implicated in adverse reactions to food additives.[1 13]

Food colours were effectively disguised in gelatin capsules, which had been rendered opaque with iron oxide and could not be distinguished from placebo. One capsule was swallowed with breakfast throughout the seven weeks of the trial. The dose of additives in the 'active' capsules was chosen so as greatly to exceed the estimated daily intake.[14] The placebo capsules contained lactose. During the seven weeks of the trial, 'active' capsules were taken daily throughout two separate weeks while placebos were taken during the remaining five weeks. Subjects were allocated randomly to one of two sequences of active and placebo weeks (table 2). The two sequences were designed to allow three clear weeks of placebo between 'active' challenge weeks with the week after an 'active' week designated a 'washout' period, when only placebo capsules were taken. Parents were informed that the weekly capsule challenges contained either food additives or placebo.

One or both parents completed a daily questionnaire of the child's behavioural and somatic symptoms throughout the trial. Ten behavioural questions were from the Conners' hyperactivity index, which is a questionnaire that has been frequently used in studies of hyperactivity.[3 15] Ten further questions were entered to assess somatic symptoms commonly associated with allergies (wheeze, urticaria, eczema, etc). Each of the above items was recorded on a 0–3 scale of severity ('not at all', 'just a little', 'quite a lot', 'a lot').

Space was provided for daily comments. An overall weekly behaviour assessment was requested from parents in which the behaviour during each week was simply recorded as 'improved', 'the same', or 'worse'.

Wilcoxon rank (paired and unpaired) tests were used where appropriate for statistical analysis.

Results

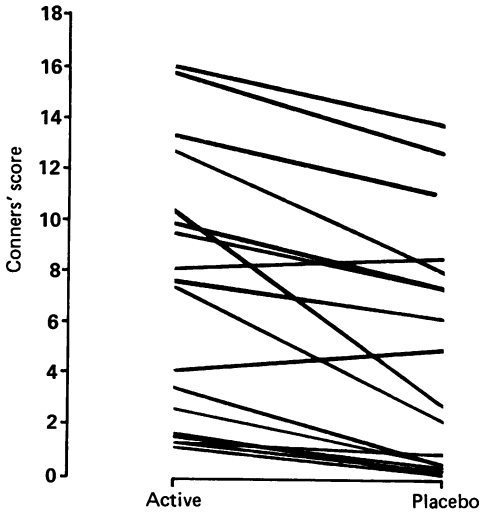
Thirty nine children were entered into the trial, of whom only 19 completed the seven weeks. There was no significant difference between those who completed the trial and those who defaulted with regard to age, sex, and atopic state.

Five children were withdrawn from the trial without having taken any capsules: one child because the family emigrated and four because the parents, on further consideration, decided not to risk provoking behaviour problems. Five sets of results were either lost in the post or mislaid. Four children were withdrawn after parents noted unacceptable behavioural changes early in the trial. On breaking the code, two children (one of whom was globally retarded) were taking active capsules and the other two were taking placebos. Six children have not yet completed the trial and seemingly will not do so as they entered the trial up to 18 months ago. The results of the 19 children who completed the trial are therefore presented.

Table 2 Study design showing the two randomly allocated challenge sequences

	Week 1	2	3	4	5	6	7
Sequence 1	A	W	P	P	A	W	P
Sequence 2	P	P	A	W	P	P	A

Week A (active): each capsule contained tartrazine (50 mg), sunset yellow (25 mg), amaranth (25 mg), and carmoisine (25 mg).
Weeks P and W (placebo and washout): each capsule contained lactose.



The mean daily Conners' behaviour score during the 14 active days and 21 or 28 placebo days. Higher scores (worse behaviour) are shown during active periods in all but two subjects. The scores are generally low. Differences between active and placebo are small but significant ($p<0·01$ Wilcoxon rank sum test).

The mean daily behavioural scores during the two 'active' capsule weeks were significantly higher than on placebo ($p<0·01$) (figure). The mean daily somatic symptom scores, however, did not differ between active and placebo ($p=0·1$) (table 3). Changes in the behavioural scores were not associated with changes in the somatic symptom scores ($p>0·5$) or with atopic state ($p>0·1$). Those of the 19 who had claimed

Table 3 The mean daily Conners' behaviour score and somatic symptom score during active and placebo weeks ($n=19$). The behaviour scores were worse during active weeks compared with placebo ($p<0·01$). No significant difference was found in somatic symptom scores between active and placebo weeks ($p=0·1$)

Case No	Mean daily behaviour score		Mean daily somatic symptom score	
	Active	Placebo	Active	Placebo
1	9·50	8·05	0·64	0·66
2	8·00	8·70	0·07	0·18
5	1·25	0·10	3·42	0·86
6	1·15	0·77	1·79	1·57
7	13·20	8·33	0·07	0
10	3·25	0·33	1·00	1·18
11	2·30	0·35	6·50	1·00
12	7·75	6·85	0·93	0·71
15	9·80	7·53	5·86	3·25
16	7·70	2·68	0·57	0
18	16·00	14·35	0·14	0·39
19	3·95	5·70	15·00	15·50
20	1·20	0·13	0	0·14
22	1·50	0	32·00	9·60
23	1·50	1·37	1·71	1·52
24	0·95	0·23	0·50	0·32
28	10·85	3·27	1·50	0·69
39	15·95	13·63	2·29	0·86
40	13·90	11·45	0·29	1·21

that additives provoked both somatic symptoms and affected behaviour were analysed separately and no significant effect of food colours on somatic symptoms was found ($p>0{\cdot}1$). In other words the changes in behaviour scores were not related to or secondary to changes in somatic scores.

There was no significant order effect between those who received active or placebo capsules first. Nor was there any difference between the scores of placebo or washout weeks, suggesting that there was little or no carry over effect from the active week into the next 'washout' week.

During the active weeks there was no difference between the behaviour scores on days 1 and 7 ($p\gg0{\cdot}25$). This finding suggests that the behavioural effect occurred early in the 'active' week giving no support to the suggestion that some food additive intolerance is the result of a cumulative effect of food additives.

A Conners' score of 15 or more has been employed in previous studies as a criterion of hyperactivity.[3 15] Only two children in the study had scores of 15 or more (that is, 15·95 and 16). The boy who had received methylphenidate after a diagnosis of the hyperkinetic syndrome completed the trial and had a mean daily behavioural score that was greater on placebo than 'active'.

Parents' overall weekly behavioural assessments (each week recorded as 'worse', 'same', 'improved') were analysed to see if they correctly identified the 'active' weeks as being 'worse'. The overall behaviour during each challenge week was compared by parents with behaviour while on an additive free diet. By excluding washout weeks, either five or six weeks remained for analysis (table 2). Two out of the 19 sets of parents did not complete any weekly assessments while one completed four out of five weeks. Table 4 shows 60/92 correct responses. Assuming that a response has a 50/50 probability of being right by chance alone, one would expect 46/92. The excess is 14 (SE 4·80), which is very significant. There is no evidence that some parents are better than others ($\chi^2_{16}=20{\cdot}95$, $p=0{\cdot}18$). If the results of each child are analysed individually after receiving two active and two or three placebo weekly challenges, however, then all the weeks must be correctly identified by each parent to achieve significance.[11] Only two parents correctly identified all the challenge weeks (table 4).

Table 4 The parental weekly behavioural assessement. Each week is recorded as 'worse', 'the same', or 'improved'. Correct assessment of active week='worse', and placebo='the same' or 'improved'

Case No	*Correct weekly assessments*
1	5/6
2	2/5
5	4/5
7	3/5
10	6/6*
11	3/4
12	1/6
15	2/6
16	3/6
18	3/6
20	5/5*
22	4/5
23	4/5
24	5/6
28	3/5
39	4/6
40	3/5

*Only two parents correctly assessed all challenge weeks.

Discussion

This study shows that a daily intake of 125 mg of a mixture of 'artificial' food colours can produce a measurable change in the behaviour scores of a group of children. This effect was unrelated to changes in somatic symptoms or to the atopic state of the children. Most parents were unable to detect the changes in behaviour at the end of each week. This disparity between the results of the behaviour scores and the parents' weekly assessments is important when it is remembered that entry into the study was based on the parents' claim to be able to detect when their children had consumed food additives. The results of the behaviour scores are not evident until somewhat time consuming calculations are performed. We believe this validates the objectivity of the challenge procedure and the methods used to monitor responses. The changes in the behavioural scores, although significant, were small (figure), and may not have been great enough for most parents to detect.

It have been claimed that it is almost impossible to disguise tartrazine challenges due to the additive's powerful colour.[4] Opaque capsules, however, provided an effective and convenient blind challenge suitable for most food additives including tartrazine (an exception may be the sulphiting agents because they probably act by the inhalation of sulphur dioxide from a solution). It is possible that the capsules were being covertly opened by parents, although this seems very unlikely as their overall weekly behavioural assessments should then have been far more accurate than was the case.

The drop out rate is disappointingly high compared with many studies of allergic diseases but is probably more typical of psychiatric studies.[16]

All but two of the children in our study attended normal schools and had no major psychiatric or neurological diagnoses. Thus this study differs from any previous studies, which involved selected groups of children who sometimes had serious and unusual concurrent problems such as epilepsy.[3 6–10] As was noted in the results, only two children could be considered hyperactive on the basis of their Conners' behaviour score. As such, the results of this study are likely to be more clinically relevant to general paediatric and allergy practice. Moreover, these children were studied without any alteration in their daily routine, rather than being admitted and challenged in an artificial laboratory or ward setting. This may be an important factor as it is known that variables such as exercise can effect the development of an allergic reaction,[17] and it is likely that other unknown variables exist.

The mechanism of food additive intolerance is uncertain. Over 3000 food additives of vastly differing chemical structure are in use, and it is unlikely that only one mechanism can account

for all reported reactions. Egger *et al* suggested an atopic mechanism was involved in hyperactivity.[3] Classical allergic reactions are unlikely to be involved, however, as there is minimal evidence of the involvement of specific antibodies,[18] and furthermore, the presence of atopy did not correlate with behavioural changes in this study.

We suggest that a pharmacological mechanism of food additive intolerance is likely. Chemical mediators such as histamine and prostaglandins are involved in food additive induced urticaria,[19] although one study failed to show any in vitro effect of tartrazine on the prostaglandin system.[20] Another study has shown that many food additives can cause histamine release from basophils.[21] In this study, doses of food colours greater than the amounts that children are likely to consume produced changes in behavioural scores that were not detected by most parents.

Previous behavioural studies have generally shown no effect of smaller doses or only suggested an effect on children under 5 years of age.[6–10] Therefore food additive intolerance may be mediated by the pharmacological release of histamine or other mediators. Behavioural effects may then result from subtle changes in pulse or skin temperature, etc, or by the action of other mediators capable of crossing the blood-brain barrier. Our own studies have shown that large doses (200 mg) of tartrazine produce small, albeit asymptomatic increases in plasma and urinary histamine in normal adults.[22] Smaller doses of tartrazine in children, on a mg per kg basis, might be expected to have a similar effect.

Hyperactive behaviour has many causes.[23] It is probable that food additives given in very large doses may act as a pharmacological trigger in a small percentage of children with behaviour problems, although even in these children the effect may be small and clinically insignificant. We feel strongly that parents of children with behavioural problems should receive a sympathetic hearing and that their ideas are not dismissed out of hand. The many factors that are known to influence behaviour need to be explained to parents, as should the limited evidence for the role of food additives and foods in causing behaviour problems. It can also be useful to explain the possible transient nature of food additive intolerance.[13] As dietary manipulation in children may result in nutritional inadequacy,[24] and may adversely affect health, it is important for a dietitian to assess children whose diets have been manipulated without professional guidance. Sometimes double blind challenges are of value clinically in showing parents that food additives are not responsible for a particular symptom. Many desperate families are unaware of the benefit of child guidance, clinical and educational psychologists, family therapy, and other helping agencies, and doctors can assist by making the appropriate referral.

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